

Clinical Research Oversight

HS

In this issue of the ACRP *Monitor*, three articles have been selected as the basis for a Home Study test that contains 30 questions. For your convenience, the articles and questions are provided in print as well as online (members only) in the form of a PDF (requires Adobe Reader and text file). This activity is anticipated to take three hours.

Answers must be submitted using the electronic answer form online (members only, \$27). Those who answer 70% of the questions correctly will receive an electronic statement of credit by e-mail within 24 hours. Those who do not pass can retake the test for no additional fee.

Hardware/Software Requirements: Home Study tests require version 4.x browsers or higher from Internet Explorer, Mozilla Firefox, or Safari. A browser that can run Adobe Flash 9.0 is required to view the digital edition of *The Monitor*, and Adobe Acrobat is required to view PDFs of the Home Study test.

The **June 2010 Monitor Home Study** is based on the following three articles in this issue:

1. Who's Watching Whom? Investigator and IRB Compliance

Terri P. Kelly, RN, MSQA, CCRA, CQA, President and Principal Consultant, GCP Compliance Auditor and Trainer, Achieve Quality, Inc.

2. FDA Warning Letters to IRBs: Who is Receiving Them and What Can Be Done to Prevent Them

Jeannine M. Ramsey, RN, BSN, CCRA, Clinical Research Monitor, IMARC Research, Inc. | David M. Vulcano, LCSW, MBA, CIP, RAC, Assistant Vice President, Hospital Corporation of America

3. Clinical Compliance: A Regulatory Perspective

Janice P. Kirby-Smith, DPharm, FRPharmS, FTOPRA, Associate Director, NDA Regulatory Science Ltd., United Kingdom

HOME STUDY LEARNING OBJECTIVES

With knowledge inferred from the articles above, respectively, learners will be able to:

1. the responsibilities of sponsors and principal investigators regarding IRB compliance, the responsibilities of sponsors and institutional review boards regarding investigator compliance, and review the U.S. Congressional committee's findings related to recent sting operations.
2. and describe the possible implications of the most common IRB Warning Letter findings issued by the FDA.
3. the regulatory aspects of clinical compliance, the role of the regulatory affairs professional, and the challenges to achieving regulatory compliance in the conduct of clinical trials.

CONTINUING EDUCATION INFORMATION

The Monitor home study tests offer ACRP, nursing, pharmacy, and continuing medical education credits.



The Association of Clinical Research Professionals (ACRP) provides 3.0 continuing education credits for the completion of this educational activity. These credits can be used to meet the certification maintenance requirement under provider number ACRP-2010-HMS-006.



Continuing Medical Education: The Association of Clinical Research Professionals (ACRP) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

ACRP designates this educational activity for a maximum of 3.0 AMA PRA Category 1 credits™. Each physician should only claim credit commensurate with the extent of their participation in the activity.



Continuing Nursing Education: The California Board of Registered Nursing (Provider Number 11147) approves the Association of Clinical Research Professionals as a provider of continuing nursing education. The CBRN program number is 11147-10-006. Each home study offering grants 3.0 nursing credits.

DISCLOSURES

The following persons who have access to influence the content of *The Monitor* have the following affiliations to disclose:

Eileen Caramanica, MS, RN, CCRA, Merck

Gary W. Cramer, ACRP

Jean Fourcroy, MD, PhD, MPH, Fourcroy Consulting

Iris Gorter de Vries, PhD, Consultant
Vikram Kumar, CCRC, Urban Estate, Phase I

Sandra O'Donnell, MA, MT(ASCP), CCRA, Clinsys

Axel Olsen, PhD, Quintiles, Inc.

Al O. Pacino II, TrainingCampus.com

A. Veronica Precup, ACRP

Andrea G. Procaccino, CCRT, CMT, Johnson & Johnson
Pharmaceutical R&D

Debbie Rosenfelder, RN, BSN, CCRC, Paragon Biomedical, Inc.

Erika Stevens, MA, Dartmouth
Hitchcock Medical Center

Linda G. Strause, PhD, Vical, Inc.

Theresa Straut, BA, CIP, RAC, Chesapeake Research Review

Lynn Van Dermark, RN, BSN, MBA, CCRA, RAC, MedTrials, Inc.

Liz Wool, BSN, CCRA, CMT, QD-Quality & Training Solutions, Inc.

**This test expires on
JUNE 30, 2011**

(original release date: 06/01/2010)

QUESTIONS 1–10

Who's Watching Whom? Investigator and IRB Compliance

- 1** The foremost ethical concern for every person working in clinical research should be:
- proper informed consent administration.
 - financial disclosure.
 - subject protection.
 - current and adequate qualifications of the investigator.
- 2** The following parties have a responsibility for ensuring that their IRB complies with applicable regulations:
- Sponsor and principal investigator
 - CRO and study coordinator
 - Study coordinator and lab personnel
 - Sponsor and central ECG readers
- 3** One reason for the sponsor to review the site's initial IRB approval letter is to:
- determine whether the IRB has been inspected by the FDA.
 - review the number of members present at the IRB meeting.
 - verify the IRB experience of the IRB members.
 - approve the release of investigational product.
- 4** In 2007, Copernicus IRB came under increased scrutiny for failure to:
- analyze the studies on an annual basis.
 - review reports of potential fraud they had received.
 - maintain their SOPs in a current manner.
 - document their review of informed consent.
- 5** Coast IRB discovered that the GAO protocol was fictitious when:
- they conducted the initial review.
 - they researched the submitted information before their review.
 - the GAO conducted the Congressional hearing.
 - the GAO requested documents prior to the Congressional hearing.

- 6** The FDA issued a Warning Letter to Coast IRB in April 2009, citing inadequate:
- risk determination
 - informed consent
 - SOPs
 - safety information

- 1 and 2
- 1 and 3
- 2 and 4
- 3 and 4

- 7** The primary purpose of an IRB is to:
- review the documents related to the trial.
 - confirm the principal investigator's qualifications.
 - protect the rights, safety, and well-being of study subjects.
 - provide regulatory advice to the sponsor.

- 8** Sponsors are responsible for:
- selecting qualified investigators
 - providing study information to the investigators
 - ensuring protocol compliance
 - consenting the subjects

- 1, 2, and 3 only
- 1, 2, and 4 only
- 1, 3, and 4 only
- 2, 3, and 4 only

- 9** Some of the findings noted by the CRA for the Ketek trial at Dr. Campbell's site were:
- discrepancies on the dates of records
 - apparent nonqualification of subjects
 - charging the subjects for research procedures
 - informed consent issues

- 1, 2, and 3 only
- 1, 2, and 4 only
- 1, 3, and 4 only
- 2, 3, and 4 only

- 10** The FDA has recently proposed amending the 312 and 812 regulations, as published in the *Federal Register*, requiring sponsors to report to the FDA any possible falsification of data within:
- 45 business days.
 - 45 calendar days.
 - 55 business days.
 - 55 calendar days.

QUESTIONS 11–20

FDA Warning Letters to IRBs: Who is Receiving Them and What Can Be Done to Prevent Them

- 11** FDA Warning Letters issued to IRBs can be located at the:
- FDA website (www.fda.gov)
 - OHRP website (www.hhs.gov/ohrp)
 - NIH website (www.nih.gov)
 - National Clinical Trial Registry Website (www.clinicaltrials.gov)

- 12** Between January 1997 and December 2009, what was the average number of Warning Letters issued to IRBs per year by the FDA?
- 89
 - 26
 - 12
 - 7

- 13** The current number of active IRBs in the U.S. is estimated to be:
- 1,500
 - 3,000
 - 5,000
 - 7,500

- 14** Findings most commonly cited in Warning Letters issued by the FDA to IRBs from 2007 to 2009 pertained to:
- written procedures
 - review of research
 - IRB membership
 - documentation of IRB activities
- 1, 2, and 3 only
 - 1, 2, and 4 only
 - 1, 3, and 4 only
 - 2, 3, and 4 only

- 15** Examples of problematic quorum or voting processes include:
- 45% of members were present
 - a physician with conflicting interest does not cast his vote
 - the only nonscientific member did not attend the meeting
 - mail-in ballots were used to vote
- 1, 2, and 3 only
 - 1, 2, and 4 only
 - 1, 3, and 4 only
 - 2, 3, and 4 only

16 According to 21 CFR 56.115, IRB meeting minutes must contain sufficient detail to show:

1. number of members voting for, against, and abstaining
2. written summary of discussions regarding controversial issues
3. general attendance
4. the time needed to review study

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

17 Expedited review is reserved for:

- A. any available IRB member with the exception of a nonscientific member.
- B. any available IRB member who has expertise in the area of study.
- C. the IRB Chairman only.
- D. the IRB Chairman or a designated, experienced reviewer.

18 A well-constructed response to a Form 483 includes:

1. how the issue will be prevented
2. a list of staff members responsible for the finding
3. how the issue identified will be corrected
4. reiteration of policies already in place

- A. 1 and 2 only
B. 1 and 3 only
C. 2 and 4 only
D. 3 and 4 only

19 If an IRB is cited for improper expedited review, an appropriate preventive action would be to:

- A. convene the board for a full review of the study in question.
- B. create a new policy that clearly defines the process for expedited review.
- C. conduct an internal audit of studies that were approved under the expedited review process to ensure compliance.
- D. circulate copies of the existing expedited review policy to the IRB membership.

20 The form signed by the principal investigator that commits him or her to assuring that the reviewing IRB fully complies with 21 CFR 56 is:

- A. Form 483
B. Form 1571
C. Form 1572
D. IRB Acknowledgement Form

QUESTIONS 21–30

Clinical Compliance: A Regulatory Perspective

21 Clinical trials are regulated at what level?

- A. National
B. Regional (EU)
C. Continental
D. Global

22 When was the EU Clinical Trials Directive adopted?

- A. 1999
B. 2001
C. 2004
D. 2007

23 Which of the following were among the intentions of the Clinical Trials Directive?

1. Increase patient safety
2. Improve study validity
3. Introduce EU centralized clinical trial authorization
4. Reduce the extent of documentation

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

24 What is the name of the EU database where protocols must be registered?

- A. EUDB
B. Eudrabase
C. EUCTbase
D. EudraCT

25 Which of the following aspects of quality of the IMP are among the most important to address?

1. Identity
2. Long-term stability
3. Purity
4. Comparison with quality of drug used in nonclinical studies

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

26 Which of the following phrases are included in the Clinical Trials Directive definition of a substantial change?

1. Likely to affect quality of the IMP
2. Likely to impact safety
3. Change validity of supporting data
4. Be otherwise significant

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

27 Which of the following activities does the regulatory affairs department need to be informed of?

1. Start of trial
2. Patient recruitment progress at each site
3. Changes to the protocol
4. End of trial

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

28 Which of the following types of study are covered by the Clinical Trials Directive?

1. Preliminary pharmacology study in humans
2. Investigation of safety of an authorized product
3. Retrospective study of a drug
4. Study on a marketed product used off-label

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

29 In the EU, which of the following are generally considered to be IMPs?

1. Test drug
2. Active comparator
3. Placebo
4. Rescue medication

- A. 1, 2, and 3 only
B. 1, 2, and 4 only
C. 1, 3, and 4 only
D. 2, 3, and 4 only

30 Which document provides information on EU labeling required for IMPs?

- A. The Clinical Trials Directive, Directive 2001/20/EC
B. Annex 13 of the GMP guideline
C. The GMP Directive, Directive 2003/94/EC
D. The Medicines for Human Use (Clinical Trials) Regulations 2004, SI 2004/1030

CORRECTIONS

Corrections to Home Studies can be found on the ACRP website and are incorporated directly into the online test.